UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/772,790 | 01/30/2001 | Endre Markovits Schersl | HAR-104 | 2203 |

7590 09/22/2004

David I. ROCHE
BAKER & McKENZIE
130 E. Randolph Drive
Chicago, IL 60601

| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/772,790 | SCHERSL, ENDRE MARKOVITS | |
| | Examiner | Art Unit | |
| | Shaojia A. Jiang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-5 and 62-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 62-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 6, 2004 has been entered.

This Office Action is a response to Applicant's request for continued examination (RCE) filed July 6, 2004, and amendment and response to the Final Office Action (mailed February 4, 2004), filed July 6, 2004 wherein claims 2, 6-35, 37-61 and 68-69 are cancelled, and claims 1, 3-5, and 62-67 have been amended. Note that claim 36 is cancelled previously.

Currently, claims 1, 3-5, and 62-67 are pending in this application.

Claims 1, 3-5, and 62-67 are examined on the merits herein.

Applicant's amendment filed July 6, 2004 with respect to the rejection of claims 1, 62, 64, and 66 made under 35 U.S.C. 112 first paragraph for containing new subject matter which was not described in the original specification and claims (i.e., "wherein the fatty acids are long chain fatty acids") of record stated in the Office Action dated February 4, 2004 have been fully considered and found persuasive to remove the

rejection since these claims have been amended to remove the new matter. Therefore, the said rejection is withdrawn.

Applicant's amendment filed July 6, 2004 with respect to the rejection of claims 1-5 and 62-68 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitation, i.e., "long chain" of record stated in the Office Action February 4, 2004 have been fully considered and found persuasive to remove the rejection since the indefinite recitation has been deleted from the claims. Therefore, the said rejection is withdrawn.

Applicant's amendment changing the limitation to the specific fatty acids in claim 1 filed July 6, 2004 with respect to the rejection of claims 1, 62, and 66 made under 35 U.S.C. 102(b) as being anticipated by Miettinen et al. (US 5,502,045) for reasons of record stated in the Office Action February 4, 2004 has been considered and found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5, and 62-67 as amended now are rejected under 35 U.S.C. 103(a) as being unpatentable over Breivik et al. (US 5,502,077, PTO-892) and Hasegawa et al. (of record) and Granja et al. (US 5,663,156, of record) and Levin et al. (US 3,031,376, of record) in view of Bundgaard (Book, "Design of prodrugs" Chapter 1, page 1, of record).

Breivik et al. discloses that the fatty acid compositions comprising the instant preferred fatty acids, eicoapentaenoic (EPA) and docashexanoic acid (DHA) with a pharmaceutically acceptable carrier, excipient, or dilutant, are known to be useful in treating or prophylaix of risk factors for cardiovascular disease such as hypercholesterolemia, hypertension, and hyperglyceridemia (see abstract, col.1 lines 14-17, Table 1-11). Note that fatty acid compositions comprising DHA and EPA in ethyl ester form such as EPA ethyl ester and DHA ethyl ester (see Example at col.11 line 30-38, and claim 12)

Hasegawa et al. discloses that the instant preferred fatty acid, linoleic acid, is known to have hypocholesteremic effect and lower the serum cholesterol levels, and therefore is useful in compositions (e.g., sunflower oil or vegetable oils known containing linoleic acid) for treating hypercholesterolemia (see the English Abstract in particular).

Granja et al. discloses that the instant preferred policosanols such as tetracosanol, hexacosanol, heptacosanol, octacosanol, and triacontanol are useful in compositions and methods for treating hypercholesterolemia and atherosclerosis (see abstract, Table 1-2 at col.3, Example 11-13 at col.12-14 and claims 1-20).

Levin et al. discloses a composition comprising one or more esters of tetracosanol, hexacosanol, octacosanol, and triacontanol, wherein the acid moiety of esters is a carboxylic acid containing from 2 to 22 carbon such as acetic acid (having 2 carbons) and propionic acid (having 3 carbons), (see particularly col.1 lines 13-17; col.3 lines 49-53 and 60-71; Example 3 at col.7 lines 19-26). Levin et al. also discloses that the composition therein further comprises food as a carrier such as vegetable oils as a liquid carrier (see particularly col. 4 lines 10-12 and 34-38). Levin et al. also discloses that the composition therein further comprises corn starch and/or lactose (known excipients) and/or vitamins (known antioxidants) (see particularly col. 4 lines 19 and 22). Levin et al. further discloses that the composition herein to be administered to human mammals and animals is for reducing anoxia, improving physical endurance, reducing fatigue, and stimulating or improving heart response (see col.3 lines 53-57).

The above cited prior art do not expressly disclose the employment of the particular fatty acids of esters, such as linoleic acid and the alcohol moiety such as tetracosanol, hexacosanol, octacosanol, and triacontanol.

Bundgaard teaches that esters of actives are most common prodrugs since esters of actives containing hydroxyl and carboxyl groups (also known as hydroxyl group in an alcohol and carboxyl group in a carboxylic acid conjugated or esterified by an ester bond) are hydrolyzed within the body (in vivo) by cleaving the ester bond to regenerate the active drug substances (see the bottom paragraph at page 1).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular carboxylic acid such as the instant

preferred fatty acid, linoleic acid, as acid moiety of esters of tetracosanol, hexacosanol, octacosanol, and triacontanol in the claimed composition herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular carboxylic acid such as the instant preferred fatty acid, linoleic acid, as the acid moiety of esters of the policosanol herein such as tetracosanol, hexacosanol, octacosanol, and triacontanol in the claimed composition herein, since discloses that the fatty acid compositions comprising EPA and/or DHA EPA, or ethyl ester and DHA ethyl ester, are known to be useful in treating or prophylaix of risk factors for cardiovascular disease such as hypercholesterolemia, hypertension, and hyperglyceridemia according to Breivik et al.

Moreover, the esters of tetracosanol, hexacosanol, octacosanol, and triacontanol having the acid moiety such as acetic acid and propionic acid are known to be useful in compositions to be administered for therapeutic purposes (e.g., stimulating or improving heart response) according to Levin et al.

Further, the instant preferred policosanol such as tetracosanol, hexacosanol, octacosanol, or triacontanol is known to be useful in compositions for treating hypercholesterolemia according to Granja et al. A fatty acid such as the instant preferred fatty acid, linoleic acid or EPA or DHA, alone is also known to be useful in compositions for treating hypercholesterolemia according to the prior art cited herein.

Furthermore, the esters herein having two moieties, the preferred policosanol and linoleic acid, or EPA or DHA, would be hydrolyzed within the body (in vivo) by cleaving the ester bond to regenerate two active drugs, the policosanol and linoleic acid,

or EPA or DHA in the body, based on the well known teachings of esters as prodrugs in pharmaceutical art according to Bundgaard.

Therefore, one of ordinary skill in the art would have reasonably expected that conjugating the policosanol such as tetracosanol, hexacosanol, octacosanol, or triacontanol with a fatty acid such as linoleic acid or EPA or DHA, into an ester in a composition to be administered, and the ester regenerating the policosanol and linoleic acid or EPA or DHA in the body after administration, both known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's arguments filed on July 6, 2004 with respect to the rejection made under 35 U.S.C. 103(a) of record stated in the Office Action February 4, 2004 have been considered but are moot in view of the new ground(s) of rejection above.

Additionally, Applicant argues that there is no basis to conclude that the above combination will yield a synergistic or superior effect compared to when they are used individually. Note that the examiner does not conclude any synergistic or superior effect

but merely additive therapeutic effects compared to when they are used individually. One of ordinary skill in the art would acknowledge that synergistic or superior effect is unexpected whereas additive therapeutic effects is expected.

Thus, as pointed out in the previous Office Action, Applicant's working Examples 1-5 of the specification at pages 8-11 herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. Examples 1-5 provide no clear and convincing evidence of nonobviousness or unexpected results over the cited prior art since there is no side-by-side comparison with the closest prior art.

Moreover, it is noted that the polycosanol esters or phytoserol-PUFA tested in Example 1-5 herein are **not** the particular fatty acids esters with the particular alcohol moiety as the instantly claimed. Thus, the evidence in the examples is also not commensurate in scope with the claimed invention. See MPEP § 716.02(d). Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The

fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner, AU 1617
September 16, 2004